protein or protein fragment, salt, electrolyte, gene or gene fragment, product of genetic engineering, steroid, adjuvant, biosealant and gas.

Please add new claim 29 as follows:

29. (New) The method of claim 16, wherein the method further comprises removing from the patient at least one encapsulated material, selected from the group consisting of a waste product, dye, indicator, nutrient, sugar, vitamin, mineral, protein or protein fragment, salt, electrolyte, gene or gene fragment, biosealant and gas.

Remarks

Applicants' response is timely filed on December 2, 2002 (since November 30th falls on a Saturday) with a 1-month extension of time to the Office Action mailed on July 30, 2002.

A typographical error, missed in the previous amendment of the paragraph on page 4, beginning at line 17, has been attended to in a second amendment of the specification. In addition the term "natural" has been added to more clearly define the di-alanine composition used by Cornelissen *et al.* Alanine compounds are known in the art to be naturally-occurring compositions of matter. Claim 1 has been amended to further define the synthetic super-amphiphilic molecules of the present invention as "wholly synthetic," and as "polymeric," and as "having a number average molecular weight ≥1400." Support for the amendment may be found in the specification, for example, at page 20, lines 13-15, and in the claims as originally filed.

Claims 1-8, 10, 13-20, 23 and 25-28 remain pending, and new claim 29 has been added, finding a basis in the specification and the pending claims. No substantive change has been made by amendment, and no new matter has been added to the application.

Response to the rejection under 35 USC §112, second paragraph.

The Examiner has rejected claims14-16, 21-23, 27 and 28 under 35 USC §112, second paragraph as being indefinite. However, Applicants' traverse the rejection for the following reasons.

Claims 15, 16, 21, 23, 27and 28 were rejected as failing to set forth any steps involved in the methods claims. However, a careful reading of the rejected claims will clearly identify the

method steps being claimed. In claim 15, a method is claimed of using the polymersome vesicle of claim 3, "wherein the method comprises transporting at least one encapsulatable material to or from the environment immediately surrounding the polymersome. "Transporting" is an active step, satisfying the requirement that a method claim must have at least one active, positive step delimiting how the claimed use is actually practiced. Similarly, in claim 16, the "transporting" step occurs wherein the environment is within a patient. Nevertheless, "transporting" is an active, positive step.

In claim 21, a method is claimed of using the polymersome vesicle of claim 15, "wherein the method comprises delivering at least one material encapsulated by the polymersome to the environment immediately surrounding the polymersome." At least one active step is identified in claim 21 as "delivering." In claim 23, the method of claim 16 "further comprises delivering at least one material encapsulated by the polymersome to the patient." Claim 27 further defines the method of claim 26, "wherein the environment is in a patient, and wherein the method further comprises exporting the encapsulatable material . . . thereby permitting its removal from the patient." Therefore, the method of claim 27 comprises at least the active steps of preparing the polymersome vesicle; encapsulating and using the polymersome, and further exporting the material.

Finally in claim 28, the method further comprises all of the foregoing steps identified in claim 27, plus an added "removing" the polymersome step. Accordingly, Applicants fail to understand why the active and positive steps as stated are inadequate in the Examiner's eyes to identify the methods being claimed. Moreover, Applicants ask the Examiner for the legal basis for making such a rejection given that each of the rejected claims meets the legal basis for a method claim.

No explanation is provided for the rejection of claim 14, and since it is not a method claim, presumably the claim was included in this particular rejection by error. If that is not the case, and the Examiner believes that claim 14 also fails to comply with 35 USC §112, second paragraph, Applicants ask for the reasoning behind the rejection.

Accordingly, since explanations have been provided and action words pointed out describing Applicants' claims, Applicants believe that the rejections under 35 USC §112, second paragraph have been rendered moot and respectfully request that the entire rejection be withdrawn.

Response to the rejection under 35 USC §101.

The Examiner has rejected claims15-16, 21, 23, 27 and 28 under 35 USC §101 as reciting a use, without setting forth the steps of the process. However, Applicants traverse the rejection for the reasons stated above, wherein the action words defining Applicants' claimed methods are carefully pointed out to the Examiner.

Moreover, claims 15, 16 and 26-28 were rejected by the Examiner as confusing because the claims recite methods comprising importing encapsulatable material from the environment immediately surrounding the polymersome and methods comprising encapsulating within a polymersome at least one encapsulatable material and using the polymersome to deliver the encapsulated material to a selected environment. In claims 16 and 27, the environment is within a patient. The polymersomes of Applicants' invention are intended to transport encapsulated materials contained therein from one environment to another. Consequently, the encapsulated material may be delivered to the environment adjacent to the polymersome (making the polymersome a delivery tool), or a material may be removed from the environment adjacent to the polymersome thus becoming encapsulated into the polymersome (making the polymersome a tool for removing materials from the surrounding environment). If those principles are applied to a polymersome administered to a patient, the patient's tissue or fluids become the environment immediately surrounding the polymersome. Thus, the polymersome may deliver an encapsulated material to the patient, or the function of the polymersome may be to encapsulate a material found in the patient so that it can be removed or excreted with the polymersome itself.

Nevertheless, in the interest of advancing prosecution of the application to allowance, the claims have been amended and this rejection rendered moot.

Claim 28 merely listed materials from which the encapsulated materials are selected. However, the Examiner questions Applicants' use of commonly understood terms in the medical arts. For instance, the difference between "drug" and "therapeutic composition" and "medicament" is questioned. A "drug" is commonly defined according to Grant & Hackh's Chemical Dictionary 5th Edition, 1987, as set forth in Applicants' previous response, as meaning "a medicinal substance . . . classified according to composition or constituents, structure or physical features, effect and use, origin and source." However, not all drugs are therapeutic compositions. For instance, insulin is a drug. It is also a therapeutic composition to a diabetic

patient; but it is not always therapeutic, since to a non-diabetic individual, its use could, in fact, be deadly. All drugs are medicaments, as is insulin. Yet, many herbs are not typically considered to be drugs, yet herbs ingested by a patient are considered to be medicaments in many cultures, and they certainly are used as therapeutic treatments. Similarly, vitamins are sold as medicaments, but they are not drugs, and although often ingested for prevention of disease, they are not necessarily therapeutic compositions.

The questions about the meanings of "nutrient," "sugar," "vitamin," and "mineral" can be answered by reviewing Applicants' previous response in which each term was defined by definitions commonly accepted in the art. Similarly, "waste product" is not a term that would be unclear to one skilled in the biological arts, or in the art of encapsulation, wherein the removal of materials by encapsulation in quite common, *e.g.*, removal of heavy metals in solution, or oils in contaminated mud flats, or metabolic waste products from an individual, each of which would be routinely viewed as a waste product by biologists, environmentalists, industrial engineers or chemists. Since the terms used by Applicants must be read as they are defined in the specification, or if not expressly defined, used as recognized in the art, the Examiner's concerns about the use of the foregoing terms seem to be misplaced and his confusion unjustified.

Accordingly, there is no basis for any confusion regarding the utility of Applicants' invention based simply upon the terms set forth above under 35 USC §101, nor is there any reason why Applicants' methods are not adequately defined in terms of the active verbs originally used in the cited claims. Applicants therefore respectfully request that for the foregoing reasons the rejections be withdrawn and the claims held to be patentable.

Response to the rejections under 35 USC §102.

The Examiner has rejected claims 1-4, 10, 13-15 and 25 under 35 USC § 102(b) as anticipated, over Ding *et al.* (*J. Phys. Chem.*, 1998) or Cornelissen *et al.* (*Science*, 1998) or Fendler *et al.* (*Science*, 1998) for the reasons of record. However, as previously stated, contrary to the Examiner's interpretation of the prior art, none of the cited references teach polymeric vesicles. Consequently, none anticipate Applicants' invention.

The Examiner argues that contrary to Applicants' arguments of record, Ding *et al.* teach vesicle formation in water or aqueous solution on p.6111, col.1. However, a careful reading of the *entire* paper by Ding *et al.*, not simply the abstract, shows that no description is provided of

vesicle formation in water. Ding *et al.* actually only describe vesicle formation in organic solvent. *After formation of the vesicle in solvent,* the membrane is crosslinked by UV-irradiation and stabilized while the vesicle is still in solvent. The formed vesicle is *subsequently* transferred to an aqueous solution that reacts and converts the exposed polyisoprene PI chains, which are hydrophobic, to hydroxylated PHI chains, which are then hydrophilic. Thus, the Ding *et al.* process is one of transfer from an organic solvent and conversion to an aqueous environment. Nowhere is it said, and nowhere would one of ordinary skill in the art read, that *direct* addition of pure copolymer in water or an aqueous solution leads to formation of vesicles.

By comparison, the membrane forming Applicants' polymersome vesicles is actually *formed in an aqueous solution.*

The Abstract of Ding *et al.* reads in relevant part as follows:

> A polyisoprene-*block*-poly(2-cinnamoylethyl methacrylate) (PI-*b*-PCEMA) sample with 88 units of isoprene and 2.3 x 10^2 units of CEMA formed vesicles in THF/hexanes with hexanes volume fractions between 50% and 95%. . . After the PCEMA shell was cross-linked, the PI chains were converted to water-soluble poly(2,3-dihydroxyl-2-methyl-butane) chains. The water-soluble hollow nanospheres uptook a large amount of rhodamine B in methanol and released the compound into water at a tunable rate depending on the amount of ethanol added to the aqueous medium.

The Introduction of Ding reads in relevant part at page 6107, col.1:

> In this paper, we demonstrate the preparation of water-soluble PCEMA-cross-linked vesicles from PI-*b*-PCEMA by modifying the PI chains chemically.

However to understand what is meant by Ding *et al.* in the "preparation of water-soluble PCEMA-cross-linked vesicles," one must read the Experimental Section. There the actual description of the vesicle preparation in organic solvent (hexane), *followed by* transfer and conversion to an aqueous environment is described as follows. The aqueous environment was not added until the step entitled "Hydroxylation of the PI Chains."

> **Vesicle Preparation.** PI-*b*-PCEMA, 400 mg, was dissolved in 65 mL of THF. A quantity of 3. 5 mL of hexanes was added. The solution was then slowly added into an equal volume of THF/HX with 85% HX to induce vesicle formation. The vesicle solution in THF/HX with 60% HX was stirred for 2 weeks before an equal volume of HX was added to yield a vesicle solution at a concentration of 1.0 mg/mL in THF/HX with 80% HX. The solution was immediately irradiated to obtain a PCEMA conversion of 40%. The vesicles were initially equilibrated in THF/HX with 60% HX, since the vesicles were found to have the narrowest size distribution at this solvent composition. More HX was added just before irradiation because it was supposed to

> increase the rigidity of the PCEMA shell (due to the reduced PCEMA swelling by THF) and reduce the degree of intervesicle fusion during the cross-linking process. The irradiated mixture was concentrated by rotor-evaporation to 12 mL.
>
> (PREPARATION OF WATER-SOLUBLE NANOSPHERES)
> **Hydroxylation of the PI Chains.** A literature method (20-22) was followed to add vicinal hydroxyl groups across a double bond in PI. This should convert PI to poly(2,3-dihydroxyl-2-methylbutane) or hydroxylated PI (PHI).
> To 8 mL of 90% formic acid (0.188 mol) at 10 °C were added mL of acetic anhydride (0.021 mol), 2 mL of 30% hydrogen peroxide (0.019 mol), and 0.06 mL of concentrated sulfuric acid. The mixture was stirred for 5 min before 6 mL of it was taken and mixed with 3 mL of the concentrated cross-linked vesicle solution (1.3 x 10-4 mol of isoprene units). The new mixture was stirred for 8 h at room temperature and then dropped into 100 mL of water. The polymer was precipitated after centrifugation and rinsed with water before it was stirred 10 mL of 1 N NaOH solution at 60 °C for 1 h. After this, the polymer was once again precipitated by centrifugation, redispersed in fresh water, and neutralized by adding 0.10 N hydrochloric acid. The precipitation and dispersion in the fresh water step was repeated another three times before the precipitate from water was dried in vacuo to obtain solid, water-soluble, hollow nanospheres.

The vesicle formation is illustrated in Figure 2 of the Ding *et al.* reference, which provides a TEM image of the PI-*b*-PCEMA vesicles prepared by the procedures described in the Experimental Section.

Hydroxylation of the PI Chains is described in the Experimental Section (page 6108, column 2) as follows:

> . . . . The strongest evidence for the conversion of PI to PHI is the water solubility of the hollow nanospheres after reacting the nanospheres with performic acid for 8 h at room temperature and hydrolyzing the sample in 1.0 M NaOH at 60 °C for 1 h.

Thus, although technically the authors indicate that their vesicles are "prepared in water" in the section entitled "Properties of the PHI-*b*-PCEMA Hollow Nanospheres," at page 6111, column1) as follows, "when first prepared in water containing NaCl salt, the PHI-*b*-PCEMA hollow nanospheres precipitated," clearly by reading the remainder of the document the actual vesicle preparation is in an organic solvent, *followed by* transfer into an aqueous solution.

Accordingly, to one of ordinary skill in the art, Applicants' direct preparation of vesicles "wherein the membrane is formed in an aqueous solution" (see Applicants' claim 1) is altogether different from vesicle preparation in an organic solvent, followed by transfer into an aqueous

solution. Applicants do not at any point in their vesicle preparation use an organic solvent, an none is suggested, which is why Applicants' resulting vesicles can immediately be used *in vivo*. The Ding *et al.* vesicles would have to be thoroughly rinsed of all solvent and converted into aqueous solution before they could be used for such purposes.

Regarding the Examiner's rejection of the claimed invention over Cornelissen *et al.* Applicants make the following comments. Cornelissen *et al.* describe a polymer composed of the natural amino acids L-alanine. In fact, they use polymers of the naturally occurring dipeptide L-Alanine-L-Alanine. However, this is not a synthetic monomer. Use of such a naturally-occurring compound leaves unanswered the question of whether a *completely synthetic* polymer can be used to make vesicles in water or any aqueous solution.

Applicants' claimed invention is restricted to polymersomes, that is, vesicles composed *entirely* of synthetic polymers (see claim 1 as amended to indicate that the vesicles are entirely synthetic). For biological applications, such as drug delivery and *in vivo* use, this is a critically important distinction because the immune system is primed to recognize natural compounds, particularly peptides. Therefore, in light of the amendment defining Applicants' polymersomes as "wholly synthetic." Applicants assert that the vesicles prepared by Cornelissen *et al.* from naturally-occurring compositions are readily distinguished from those of the present invention.

In response to the Examiner's rejection of the presently claimed invention over Fendler, 1984, Applicants' point out that Fendler teaches only small amphiphiles (lipid-like in molecular weight) with no more than four covalently crosslinkable bonds. However, neither Fendler, nor any other reference regarding such amphiphiles, describes *polymeric* vesicles of the type disclosed in the present invention, which remain intact following either a cycle of dehydration and rehydration, or exposure to organic solvents (see, present application at page 3, lines 1-9). By comparison, Applicants' polymersome membranes made from super-amphiphilic copolymers that incorporate an effective number of crosslinkable groups per copolymer are crosslinked into a contiguous, semi-permeable membrane.

As proof of thorough crosslinking in the vesicles of the present invention, polymersomes with crosslinked membranes remain as intact vesicles, maintaining their encapsulated contents, after at least one cycle of dehydration and rehydration or exposure to organic solvents, such as chloroform (see, *e.g.*, FIG. 10, FIG. 11 or the specification at page 33, lines 10-14). Applicants' vesicles comprise "amphiphilic molecules that are polymeric," and also have "a number average

molecular weight ≥1400." Thus Applicants' polymersomes are far larger than the four, covalently, cross-linkable bond lipid-like materials taught by Fendler, even if such materials were truly vesicles, which they are not. Consequently, the amphiphiles taught by Fendler do not anticipate the crosslinked membrane of the polymersome vesicles of the present invention. Nor can such small lipid-like molecules anticipate Applicants' polymeric invention as a whole, particularly in light of the amendment defining Applicants' amphiphilic molecules as expressly "having a number average molecular weight ≥1400."

Consequently, it is clear that each of the cited references fails to anticipate Applicants' invention under 35 USC § 102(b) since none teach the polymeric vesicles of the present invention. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Examiner has also rejected claims 1-4, 6, 10, 13-18 and 25 as being anticipated by Hentze (*Macromolecules,* 1999) and claims 1-2, 7-9, and 14-18 as being anticipated by Liu (*Macromolecules,* 1999) under 35 USC § 102(a). For the reasons of record stated in Applicants' previous response, however, neither of the cited references teaches a vesicle formed in accordance with the methods of the present invention to produce Applicants' polymersomes. Neither manuscript meets the criteria stated, for example, in Applicants' specification at page 14, that a vesicular structure must comprise a membrane, which separates an internal solution from an external solution. However, rather than reiterate the reasons why the cited references are distinguished from the present invention, Applicants incorporate herein the reasons of record.

Nevertheless, as pointed out in Applicants' Response to the Office Action mailed December 20, 2001 and entered into the record with the Request for Continued Examination filed May 20, 2002, neither of the cited manuscripts can be considered "prior art" to Applicants' invention. Therefore, neither can render Applicants' invention unpatentable.

The Hentze manuscript indicates that it was first received for review by *Macromolecules* on March 18, 1999 – see page 5803, following the naming of the authors, but before the Abstract. By comparison Applicants' invention was conceived and reduced to practice before the earliest possible date accorded to the Hentze manuscript. In fact, Applicants' manuscript corresponding to the present application was reviewed for publication in *Science* (Discher *et al.*, 1999) in January 27, 1999, (although not accepted following review until April 5, 1999 – see Discher *et al., Science* 284:1143-1146 (May 14, 1999) (cited in Applicants' IDS as reference I). Therefore, Applicants' invention had already been reduced to practice and written for review by

at least January 27, 1999, several months before the earliest possible date of March 18, 1999 of the Hentze manuscript. Given the clear factual statement of each of the foregoing dates in the Hentze publication and Applicants' own publication, no Declaration appears to be needed to antedate the cited reference, although Applicants' will prepare such Declaration if the Examiner so requires. Accordingly, Hentze is not "prior art."

SImilarly, the Liu manuscript was received for review by *Macromolecules* on April 8, 1999 – see factual statement following the naming of the authors, but before the Abstract. By comparison Applicants' manuscript was reviewed for publication in *Science* (Discher *et al.*, 1999) as stated above on January 27, 1999, several months before the earliest possible date of the Liu manuscript. As indicated above, Applicants' are merely directing the Examiner to factual information printed on the face of the cited manuscript, and no Declaration antedating the cited reference appears to be necessary. Accordingly, Liu is not "prior art." Accordingly, Applicants respectfully request that the claims be reconsidered and that the rejections under 35 USC § 102(a) as being anticipated by Hentze or Liu be withdrawn, and the claims found allowable.

Response to the rejection under 35 USC §103(a)

The Examiner has rejected claims 3-8, 10 and 14-20, 23, and 25-28 under 35 USC § 103(a) as obvious, over Ding (*J. Phys. Chem.*, 1998), Fendler (*Science*, 1998) or Hentze (*Macromolecules,* 1999) for the above-stated reasons, and for those of record. In making this rejection, the Examiner states that each of the cited references suggests potential applications of polymeric vesicles for drug delivery. However, for Applicants' reasons of record and the foregoing arguments, Applicants resprectfully submit that none of the cited references discloses or even suggests the formation of a polymeric vesicle, let alone links how such non-disclosed vesicles could be used for drug delivery. As a result, for the above-identified reasons that the cited references were alone unable to anticipate the present invention, they fail to render Applicants' invention obvious when combined. Even if combined, and further combined with the knowledge of the art at the time of the invention, gaps remain unfilled that could make Applicants' invention obvious to one of ordinary skill in the art with any expectation of success without undue experimentation. These deficiencies cannot been met by combining the references that each failed to stand alone to teach Applicants' invention. Each cited reference fails to teach or suggest Applicants' polymeric vesicles. Thus, even when combined, they cannot

teach the formation of a polymeric vesicle, or Applicants' use thereof; and they cannot render Applicants' invention obvious.

The Examiner asserts that "all of the references cited clearly teach the application of these polymers for drug delivery." However, although the references may have a goal of using the disclosed structure in each for drug delivery, each fails to suggest, even if combined, Applicants' invention, defined as a polymersome vesicle comprising a semi-permeable, thin-walled encapsulating membrane, wherein the membrane is formed in an aqueous solution, and wherein the membrane comprises one or more synthetic super-amphiphilic molecules. Consequently although the cited references may propose methods for drug delivery, none render Applicants' claimed invention obvious because none accomplish drug delivery by controlled release from a polymeric vesicle as defined by Applicants in their claimed invention.

Accordingly Applicants again point to the overwhelming differences between the prior art configurations and that of the present invention, none of which are met by the references relied upon by the Examiner. The present invention quite simply operates in a completely different manner from the prior art, and produces wholly synthetic, polymeric vesicles of a size that permits a multitude of uses, none of which have been previously possible. Thus, the prior art fails to render Applicants' invention obvious, and Applicants respectfully request that in light of the foregoing, the rejection under 35 USC § 103(a) be reconsidered and withdrawn.

In sum, Applicants assert that all pending claims are in condition for allowance, and respectfully request that allowance be granted at the earliest date possible. Should the Examiner have any questions or comments regarding Applicants' amendments or response, he is asked to contact Applicants' undersigned representative at (215) 575-7034.

Respectfully submitted

Date: December 2, 2002

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Version with markings to show changes made

In the specification:

Paragraph at page 4, lines 17-29 has been amended for the second time as follows:

Many [~~wholly~~] semi- or partially- synthetic, amphiphilic molecules are also significantly larger (in molecular weight, volume, and linear dimension) than phospholipid amphiphiles, and have therefore been called "super-amphiphiles" (Cornelissen *et al., Science* 280:1427 (1998)). Cornelissen *et al.* used polystyrene (PS) as a hydrophobic fraction in their series of non-synthetic, natural block copolymers designated PS40-b-(isocyano-L-alanine-L-alanine)y. For y = 10, but not y = 20 or 30, loop structures, referred to as small collapsed vesicles, having diameters ranging from tens of nanometers to several hundred, and a bilayer thickness of 16 nanometer were mentioned as existing under a single acidic buffer condition (0.2 mM Na-acetate buffer, pH 5.6). However, bilayer filaments and superhelical rods existed, without explanation, under the same solution conditions, thus making the stability of the collapsed vesicles, relative to the other microstructures, highly uncertain for the studied dipeptide-based copolymer. Furthermore, no demonstration of semi-permeability was reported, and reasons for apparent vesicle collapse were not given, further raising questions of vesicle stability.

In the claims:

Claims 1, 15, 16 and 26-28 have been amended as follows:

1. (Twice Amended) A polymersome vesicle comprising a semi-permeable, thin-walled encapsulating membrane, wherein the membrane is formed in an aqueous solution, and wherein the membrane comprises one or more wholly synthetic super-amphiphilic molecules that are polymeric, having a number average molecular weight ≥1400.

15. (Thrice Amended) [~~A~~] The method of using the polymersome vesicle of claim 3, wherein the method comprises:

preparing the polymersome vesicle; and

importing into the polymersome at least one encapsulatable material from the environment immediately surrounding the polymersome[~~,~~]; and

transporting the polymersome and the at least one material encapsulated therein away from the surrounding environment, thereby [~~encapsulating the at least one material within the polymersome and~~] removing it from ~~the surrounding~~ said environment.

16. (Thrice Amended) The method of claim 15, wherein the environment is [~~in~~] a patient, and wherein the method further comprises ~~importing the encapsulatable material to [or from] the patient, thereby permitting delivery to~~] removing the polymersome and the at least one material encapsulated therein from the patient.

26. (Amended) [~~A~~] The method of using the polymersome vesicle of claim 3, wherein the method comprises:

preparing the polymersome vesicle;

encapsulating therein at least one encapsulatable material; [~~and~~]

[~~using~~] delivering the polymersome [, ~~which comprises~~] comprising the at least one encapsulated material to a selected environment; and

releasing [~~, for exporting~~] said encapsulated material(s) [~~contained therein~~] into the environment immediately surrounding the polymersome.

27. .(Amended) The method of claim 26, wherein the environment is [~~in~~] a patient, and wherein the method further comprises [~~exporting the encapsulatable material from the patient into the polymersome, thereby permitting its removal from~~] delivering the polymersome and the at least one material encapsulated therein to the patient, and releasing the encapsulated material therein.

28. (Amended) The method of claim 27, wherein the method further comprises [~~removing the polymersome and the material encapsulated therein from~~] releasing to the patient at least one encapsulated material, ~~wherein the encapsulated material is~~ selected from the group consisting of a drug, therapeutic composition, medicament, dye, indicator, nutrient, sugar, vitamin, mineral, protein or protein fragment, salt, electrolyte, gene or gene fragment, product of genetic engineering, steroid, adjuvant, biosealant and gas.

Claim 29 is newly added.